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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/701,064	11/05/2003	H. William Bosch	029318-0978	6295

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EXAMINER	
TRAN, SUSAN T	
ART UNIT	PAPER NUMBER
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/701,064	BOSCH ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 17-90* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-35 and 76-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The claims are rejected because they do not identify the structure, material, or acts set forth in the specification that would be capable of carrying out the functional properties recited in the claims. It appears from the specification that the claimed properties are achieved from several specific formulations that contain specific structures, such as dosage core with coating layers that comprise specific ratios of film forming polymers, or tablet contains specific excipient (examples 1-4). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Accordingly, the structure which makes up the formulation must be clearly and positively specified.

Claims 25-35 and 76-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims lack the description of the possible genus with the recited functional characteristics.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 and 17-57 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-75 of copending Application No. 10/619539 ('539). Although the conflicting claims are not identical, they are not patentably distinct from each other because application '539 claimed a stable particulate composition comprising: (a) particles of at least one active agent having an effective average particle size of less than about 2000 nm; and (b) at

least one surface stabilizer. Glipizide is found in claims 31 and 75. Surface stabilizer is found in claims 19-21, 23 and 24. Excipient is found in claim 22. The method of making the composition is found in claim 46. Thus, the present claims are anticipated by the claims of the '539 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-15 and 17-57 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 09/337675 ('675). Although the conflicting claims are not identical, they are not patentably distinct from each other because application '675 claimed a solid dose particulate composition comprising: (a) a particulate drug composition comprising a poorly soluble particulate drug to be administered and at least one surface stabilizer associated with the surface of the particulate drug, wherein the particulate drug has an effective average particle size of less than about 1000 nm, wherein at least 50% of the drug particles have an average particle size of less than about 1000 nm; and (b) at least one pharmaceutically acceptable rate-controlling polymer. Surface stabilizer is found in claim 37. Glipizide is found in claim 52. Thus, the present claims are anticipated by the claims of the '675 application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 10, 11, 13-15, 17-35, 40-43, 45-50, 52, 53, 55-65, 67, 68 and 70-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liversidge et al. US 5,145,684, in view of Kuczynski et al. US 5,024,843.

Liversidge teaches a dispersible particle comprising from about 0.1-60% crystalline drug substance, and from about 0.1 to about 90% surface modifier. The particle has an effective average particle size of less than about 400 nm (abstract; column 2, lines 31-43; and column 5, lines 65 through column 6, lines 1-5). Suitable drug substance includes anti-diabetic agents (column 3, lines 57-58). Surface modifier includes hydroxypropyl cellulose (column 4, lines 34-63). Liversidge further teaches a method for preparing the dispersible particle comprising dispersing a drug substance in a liquid dispersion that contains surface modifier to form a premix, homogenizing the premix, and subjecting the premix to grinding media (column 5, lines 41 through column 6, lines 1-17). The obtained dispersion of surface modified drug nanoparticles is combined with pharmaceutical excipient to form pharmaceutical formulation for oral, rectal, injection administration, and the like (column 7, lines 48-64).

Liversidge does not explicitly teach the claimed active, such as glipizide.

Kuczynski teaches anti-diabetic drug includes glipizide in a dosage form for administration to patients in need of glipizide therapy (abstract). Kuczynski further teaches glipizide is known to lower blood glucose, and is useful for patients with non-insulin dependent diabetes mellitus (column 1, lines 45-20). Thus, it would have been obvious to one of ordinary skill in the art to select glipizide as an anti-diabetic agent in view of the teaching of Kuczynski, because Kuczynski teaches glipizide is a known antidiabetic agent in pharmaceutical art, and because Kuczynski teaches glipizide is odorless and advantage antidiabetic agent useful for the treatment of diabetes.

It is noted that the cited references do not expressly teach the claimed properties, such as the T_{max}, C_{max}, AUC, and release profiles. However, it is the position of the examiner that the composition taught by the cited references would have the properties similar to that of the claimed properties, because the references teach the use of the claimed surface modifying agent hydroxypropyl cellulose to obtain a surface modified nanoparticle having effective particle size of less than 400 nm. It is noted that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claims 9, 12, 44, 51, 54, 66 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liversidge et al. US 5,145,684, in view of Kuczynski et al. US 5,024,843 and Parikh et al. WO 98/07414.

Liversidge and Kuczynski are relied upon for the reason stated above. The references do not teach the steps in claim 44, as well as the use of at least two surface stabilizers.

Parikh teaches a composition comprising microparticles of water-insoluble drugs and method for preparing same (abstract). The composition comprises the use of combination of surface modifiers and a phospholipid (page 3, lines 4-16). The method comprises mixing the insoluble drugs particle with phospholipid and precipitating from a dissolved mixture of the substance, phospholipid and surfactant followed by sonication, milling, homogenization, and solvent precipitation (page 8, first paragraph). Thus, it would have been obvious to one of ordinary skill in the art to modify the method of Liversidge using the steps in view of the teaching of Parikh, because Parikh teaches a method suitable to prepare water-insoluble drugs that converts lipophilic to hydrophilic surfaces with increased steric hindrance/stability, and possibly modify zeta potential of surfaces with more chare repulsion stabilization (page 3, last paragraph).

Response to Arguments

Applicant's arguments filed 01/10/07 have been fully considered but they are not persuasive.

Applicant argues that the main feature of the glipizide particles recited in the claims of the present application is that they have an effective average particle size of less than about 2000 nm. This effective average particle size provides the compositions of the invention with a specific pharmacokinetic profile as recited in the claims. However, in response to applicant's argument, the present specification does not provide any evident that the claimed effective average particle size of less than about 2000 nm results in the claimed pharmacokinetic profile. The specification discloses that the invention *preferably* provides glipizide compositions having a *desirable* pharmacokinetic profile when administered to mammalian subjects. *The desirable* pharmacokinetic profile of the glipizide compositions *preferably* includes, but is not limited to: (1) a T_{max} for glipizide, when assayed in the plasma of a mammalian subject following administration, that is preferably less than the T_{max} for a non-nanoparticulate glipizide formulation administered at the same dosage; (2) a C_{max} for glipizide, when assayed in the plasma of a mammalian subject following administration, that is preferably greater than the C_{max} for a non-nanoparticulate glipizide formulation administered at the same dosage; and/or (3) an AUC for glipizide, when assayed in the plasma of a mammalian subject following administration, that is preferably greater than the AUC for a non-nanoparticulate glipizide formulation administered at the same dosage. It is known in pharmaceutical art that pharmacokinetic, including T_{max}, C_{max}, AUC, and release profiles are the properties depend in many different factors in the dosage form, such as the coating, the polymers use, the particle size of the active ingredients, the amount of the ingredients, and/or the solubility of the active compounds.

Specification does not provide any example showing the claimed pharmacokinetic of the present invention is solely due to the effective average particle size alone. Accordingly, one of ordinary skill in the art would not be able to make and/or use the claimed invention without an undue experimentation. It is noted that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). Accordingly, the 112, first paragraph rejection is maintained.

Applicant argues that there is no motivation combine Liversidge with Kuczynski, because Liversidge teaches a lengthy list of classes of drugs, including antidiabetic agents, that could be used to form a nanoparticulate active agent composition. However, Liversidge makes no mention of glipizide, nor are antidiabetic agents even a "preferred" class of drugs. Thus, Liversidge fails to teach or suggest nanoparticulate glipizide compositions.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Liversidge recognizes the need in pharmaceutical art to obtain formulations having high bioavailability. Liversidge teaches method and formulation useful for active agents

known to have low water-solubility including anti-diabetic compound. Kuczynski teaches that glipizide is an anti-diabetic compound known to have a very low water-solubility (see Kuczynski at column 1, lines 25-35). Kuczynski teaches the desirability to obtain a formulation of glipizide useful in pharmaceutical art for the treatment of diabetes. Accordingly, one of ordinary skill in the art would have been motivated to, by routine experimentation determine a suitable method in view of the teaching of Liversidge to process/formulate glipizide compound into a formulation useful in pharmaceutical art.

Claims Allowable

Claim 16 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S. Tran

SUSAN TRAN
PRIMARY EXAMINER